Paper No. 32

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte REID VON BORSTEL,
JAN M. CASADEI, BALREDDY KAMIREDDY,
JOHN KENTEN, MARK T. MARTIN,
RICHARD J. MASSEY, DAVID M. SIMPSON,
RODGER SMITH, RICHARD C. TITMAS,
RICHARD O. WILLIAMS, and ANDREW D. NAPPER

Appeal No. 2000-0893[1]
Application No. 08/392,407

ON BRIEF[2]

Before SCHEINER, ADAMS, and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 80-150 which are all the claims pending in the application.

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[1] This appeal is related, through at least one common parent application, to Appeal No. 2001-1910 (Application No. 08/325,540), and Appeal No. 2001-1957 (Application No. 08/479,849). Accordingly, these appeals were considered together.

[2] Pursuant to appellants request (Paper No. 43, received February 26, 1999) an oral hearing for this appeal was scheduled for December 13, 2001. However, we note that appellants waived (Paper No. 31, received November 16, 2001) their request for oral hearing. Accordingly, we considered this appeal on Brief.

Claim 80 is illustrative of the subject matter on appeal and is reproduced below:

80. A catalytic antibody raised to a hapten of formula I

$$G\text{-}F\text{-}(CH_2)_n\text{-}E\text{-}D\text{-}B\text{-}A\text{-}X \quad (I)$$

wherein:

X is

(a) a nucleoside analog joined at the 5′ and/or 3′ position of the aldose ring wherein the hydroxyl groups on the sugar moiety of the nucleoside analog are unsubstituted, independently substituted with acyl, phosphate and alkyl radicals, or replaced with H, halogen or azide, and wherein the O of the nucleoside by which it is attached can be replaced by S, NH, or CH_2,

(b) $QP(O)(NH_2)NR^1R^2$, wherein Q is O or CH_2, or Q can be omitted, and R^1 and R^2 are the same or different but both cannot be H and each is haloalkyl, alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene, or R^1 and R^2 are connected to each other in a ring structure such as morpholino or piperidine,

(c) melphalan joined to the remainder of the compound at a primary amino group, or melphalan joined to the

remainder of the compound at a primary amino group wherein the primary amino group can be replaced by CH_2 or S; or

(d) daunomycin or other drug joined to the remainder of the compound at a hydroxy, amino or thio group which can be replaced by CH_2, S, or O;

A, which may be omitted, is ethylene or any isomer of propenyl;

B, which may be omitted, is O, S, CH_2, or NR^3, wherein R^3 is H, alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene;

D, which may be omitted, is

(a) C=O,

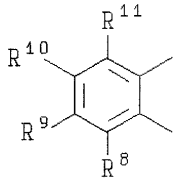
(b) $C=NR^4$ or $R^5R^6N-C=NR^4$, wherein R^4 is H, alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene, R^4 and R^5 or R^5 and R^6 can be connected to each other in a ring structure such as morpholino or piperidine, or R^5 and R^6 can be haloalkyl, alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene,

(c) SO or CHOH with any stereochemistry,

(d) SO_2, or

(e) $P(T)(TR^7)$ wherein T is O, N, S or CH_2 and R^7 is H, alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene and is unattached or attached to E at R^8, R^{11} or R^{13};

E, which may be omitted, is the radical



or $R^{12}R^{13}C$ wherein R^{8-13} are the same or different and are H or alkyl with 1-10 carbon atoms, phenyl, substituted phenyl, alkene with 1-10 carbon atoms, hydroxyalkyl, alkoxy, aminoalkyl, aklylthio, thioalkyl, amino, aklylamino, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium, carboxylate, sulfate, phosphate, or hydroxyl, and wherein R^{12} and R^{13} are the same or different and are O substituted with alkyl, alkyl with heteroatoms, cycloalkyl, phenyl, substituted phenyl, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium or alkene, or R^{8-13} are connected to each other in a ring structure

such as a five-membered or six-membered acetal ring where the diol is derived from a sugar, cycloalkyl or phenyl moiety, and is unattached or attached to the radical D at R^7 through R^8 or R^{11} or R^{13};

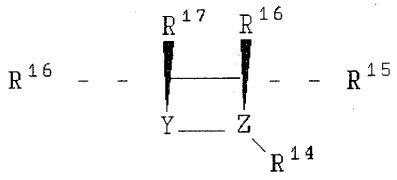
n is an integer from 0 to 3;

F, which may be omitted, is an oxygen, carbonyloxy, or oxycarbonyl radical; and

G, which may be omitted, is

(a) H or alkyl with 1-10 carbon atoms, alkoxy with 1-10 carbon atoms, phenyl, substituted phenyl, alkene with 1-10 carbon atoms, hydroxyalkyl, aminoalkyl, thioalkyl, amino, alkylamino, alkylphosphonate, alkylsulfonate, alkylcarboxylate, alkylammonium, carboxylate, sulfate, phosphate, or hydroxyl, or

(b) the radical



wherein Y is C=O, SO_2, CHOH or SO with any stereochemistry, Z is O, N, CH with any stereochemistry, or S, and R^{14}, R^{15}, R^{16}, R^{17} or R^{18} is the site of attachment to the remainder of the compound, provided that where R^{14} is the site of attachment, then R^{15}, R^{16},

R^{17}, and R^{18} are the same or different and are hydrogen, alkyl with 1-10 carbon atoms, alkenyl with 1-10 carbon atoms, phenyl, substituted phenyl, carboxylalky with 1-10 carbon atoms which is unsubstituted or substituted by a heterocyclic ring or phenyl ring, said rings being unsubstituted or substituted, alkoxy with 1-10 carbon atoms, alkylamino with 1-10 carbon atoms, aminoalkyl with 1-10 carbon atoms, acyloxy with 1-10 carbon atoms which is unsubstituted or substituted by a heterocyclic ring or a phenyl ring, said rings being unsubstituted or substituted, or acylamino with 1-10 carbon atoms which is unsubstituted or substituted by a heterocyclic ring or a phenyl ring, said rings being unsubstituted or substituted, and further provided that where one of R^{15}, R^{16}, R^{17}, or R^{18} is the site of attachment, then R^{14} and the remainder of R^{15}, R^{16}, R^{17}, and R^{18} are the same or different and are as defined for R^{15}-R^{18} above when R^{14} is the site of attachment and R^{14} is either SO_3H or SO_4H,

said catalytic antibody being capable of catalytically enhancing the rate of cleavage of a drug X or B-A-X, wherein B, A, and X are defined as above, from a residue of a prodrug of formula I, wherein said catalytic antibody exhibits catalytic activity which corresponds to activities exhibited by a protease selected from the group consisting of an esterase, an amidase, an acetal hydrolase and a glycosidase.

Janda et al. (Janda), "Substrate Attenuation: An Approach to Improve Antibody Catalysis," Tetrahedron, Vol. 47, No. 14/15, pp. 2503-2506 (1991)

The references relied upon by appellants are:

Schechter et al. (Schechter), "Preferential Formation of Antibodies Specific toward D-Amino Acid Residues upon Immunization with Poly-DL-peptidyl Proteins," Biochemistry, Vol. 6, No. 3, pp. 897-905 (1967)

(Sambrook), Molecular Cloning, a laboratory manual, Volume 3, pp. 18.1-18.8 (E.F. Sambrook et al. eds., 2nd ed., Cold Spring Harbor Laboratory Press 1989)

GROUNDS OF REJECTION

Claims 80-150 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claimed invention.

Claims 80, 109, and 120 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite in the recitation of the phrase "which corresponds to activities exhibited by a protease selected from the group consisting of: an esterase, an amidase, an acetal hydrolase and a glycosidase."

We affirm the rejection under 35 U.S.C. § 112, second paragraph, and reverse the rejection under 35 U.S.C. § 112, first paragraph.

DISCUSSION

The rejection under 35 U.S.C. § 112, first paragraph:

Initially, we recognize and agree with appellants' statement (Brief, page 14) "that a working example is not required for enablement." See In re Strahilevitz, 668 F.2d 1229, 1232, 212 USPQ 561, 563 (CCPA 1982) (working examples are not required to satisfy section 112, first paragraph.).

The enablement rejection of record is concerned with whether the specification teaches "the preparation of even one catalytic antibody." Answer, page 3. To satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, a patent application must adequately disclose the claimed invention so as to enable a person skilled in the art to practice the invention at the time the application was filed without undue experimentation. Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1371-72, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999). We note, however, that "nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). As set forth in In re Wright, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993):

> When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement.

While the examiner acknowledges (Answer, page 5) appellants' reference (Brief, page 11) to Sambrook and agrees (Answer, page 5) that with the appropriate carrier molecule "an antibody can be made to virtually any chemical compound," the examiner finds (Answer, pages 4-5), with reference to the factors set forth in In re Wands, 858 F.2d 731, 737,]8 USPQ2d 1400, 1404, (Fed. Cir. 1988):

> that the quantity of experimentation would be high because there is no direction or guidance presented as to which haptens will produce catalytically active antibodies and which will not. The guidance given for making catalytic antibodies is only as to possible screening methods. It is well known in the catalytic antibody art that exactly what hapten is used will determine whether the antibody will be catalytically active or not. As there are no working (or non-working) examples showing which haptens will be operable and which will not …, the prior art teaches that what hapten is used is paramount in whether a given hapten will produce a catalytic antibody the predictability of this art is not great … and the claims are very broad….

In support of this position, the examiner relies (Answer, page 5) on Schultz and Janda.[3] According to the examiner (id.) "[t]hese references show that whether an antibody that has catalytic activity is obtained from the many

[3] We note that the examiner relied, inter alia, on Schultz and Janda, in the Final Office Action, to support a rejection under 35 U.S.C. § 103. This rejection, however, was subsequently withdrawn. See Answer, page 7. The examiner, however, did not rely on these references in the Final Office Action to support the rejection under 35 U.S.C. § 112, first paragraph. For emphasis, we note the examiner's statement (Answer, page 5) that "these references merely reinforce … [the] argument [of record] and do not constitute a new ground of rejection." In this regard, we note as set forth in In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n.3 (CCPA 1970) ("[w]here a reference is relied on to support a rejection, whether or not in a 'minor capacity,' there would appear to be no excuse for not positively including the reference in the statement of the rejection"). Under these circumstances, we would not generally consider these references as new applied to the rejection under 35 U.S.C. § 112, first paragraph. However, on this record appellants have responded (Reply Brief, pages 8-10) to the examiner's newfound reliance on Schultz and Janda. Accordingly, we will consider the position of both the examiner and appellants as it relates to Schultz and Janda.

antibodies produced is dependent upon exactly what hapten is used and that is not readily predictable." Specifically, the examiner finds (id.), Janda teach "catalytic antibodies were raised against hapten (1) and … found that substrates with the greatest homology to the [sic] hapten (2 and 3) were not hydrolyzed by the antibody, whereas substrates that had less homology to the hapten (4-6) were hydrolyzed. Similarly, the examiner finds (Answer, pages 5-6), "[i]n Schultz catalytic antibodies made using a mixture of diastereomers of a hapten (I) catalyzed the cleavage of the D diastereomer of a homologous substrate (II) but not the L diastereomer, even though the hapten used was a mixture of both diastereomers."

In view of this evidence, the examiner concludes (Answer, page 6) "that due to the unpredictability of the catalytic antibody art and the fact that not one example of an operable catalytic antibody is contained in the instant specification, the instant claimed invention would require undue experimentation…." In response appellants find (Reply Brief, pages 8-9) that Schultz and Schechter, which is cited by Schultz, demonstrate that:

> one of ordinary skill in the art would reasonably predict that a mixture of enantiomers would necessarily yield a mixture of antibodies which are preferentially specific for the D-isomer. Therefore, one would also predict that those catalytic antibodies identified would be active against the D-isomer rather than the L-isomer. This is, in fact, what Schultz found. Given Schechter's observations, one would reasonably predict that an enantiomeric mixture of haptens would preferentially produce catalytic antibodies that stereospecifically catalyze the conversion of the D-isomer in an enantiomeric mixture.

Similarly, appellants find (Reply Brief, pages 9-10) that "Janda shows how one can control the reaction catalyzed by considering the different elements

present in the hapten and substrate. … In this regard, Janda only lends credence to the operability of the present invention, rather than demonstrating its unpredictability."

We note that the examiner failed to respond to appellants' arguments concerning Janda and Schultz. We also note that appellants incorporate by reference (see Specification, pages 9 and 10) three United States Patents that describe the catalysis of chemical reactions by antibodies, and the use of transition state analogues to immunize animals and the production of catalytic antibodies. However, we find no discussion by the examiner on this record as to why these patents and the other documents referred to in this section are insufficient evidence that a person of ordinary skill in the art would have been able to practice the claimed invention as filed. In this regard, we remind the examiner that "a patent need not teach, and preferably omits, what is well known in the art" Hybritech Incorporated v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). On the record before us the examiner made no attempt to explain why appellants' specification and the prior art relied upon, and incorporated by reference therein is insufficient to enable appellants' claimed invention. Instead, it appears on this record that the examiner has simply concluded that the specification does not support the claimed invention, and makes reference to Janda and Schultz, after prosecution is closed, in an effort to support this conclusion.

We must emphasize that it is the examiner's burden to first demonstrate that the claimed invention is not supported by an enabling disclosure. As set forth in In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) it:

> is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

On reflection, given the examiner's failure to address the specific teachings provided in the specification, including the documents incorporated by reference therein, and his failure to address appellants' position with regard to Janda and Schultz, we are compelled to agree with appellants' position (Reply Brief, page 10) that "the [e]xaminer has failed to effectively challenge the presumptive validity of the present invention…." Stated differently, in our opinion, the examiner failed to meet his burden to establishing a prima facie case of non-enablement.

Accordingly, we reverse the rejection of claims 80-150 under 35 U.S.C. § 112, first paragraph.

THE REJECTION UNDER 35 U.S.C. § 112, second paragraph:

The examiner finds (Answer, page 6) "[t]he instant claims are indefinite and confusing in the recitation of 'which corresponds to activities exhibited by a protease selected from, the group consisting of: an esterase, an amidase, an acetal hydrolase and a glycosidase' …." According to the examiner (Answer, pages 6-7):

> Proteases do not consist of any of the recited enzymes, rather proteases are enzymes specific for the cleavage of peptide bonds whereas esterases cleave esters, amidases cleave amides, acetal hydrolases cleave acetal groups and glycosidases cleave glycosyl compounds. All of the recited enzymes are hydrolases and if 'a protease' was [sic] changed to 'a hydrolase' or 'an enzyme' then this rejection would be dropped.

We find no error in the examiner's position. In addition, appellants concede to the examiner's position, stating (Reply Brief, page 14) that "[a]ppellants thank the [e]xaminer for his helpful suggestion and agree to such an amendment pending the outcome of this appeal." Accordingly, we affirm the rejection under 35 U.S.C. 112, second paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

Toni R. Scheiner Administrative Patent Judge	)
	) BOARD OF PATENT
Donald E. Adams Administrative Patent Judge	) APPEALS AND
	) INTERFERENCES
Demetra J. Mills Administrative Patent Judge	)

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